REMARKS

Claims 23, 25-31 and 33-70 are pending in this application.

The claims encompass, *inter alia*, the uses of a specific compound for a specific treatment, that is, methods for inhibiting the formation or growth of tumors in humans recited in claim 23, methods for inhibiting metastasis of tumors in humans recited in claim 41, and methods for reducing the recurrence of tumors in humans recited in claim 49, using an effective amount of thalidomide. The claims further recite methods that employ specific doses, specific dosing regimens, specific tumors and specific patients, as recited in claims 25-31, 33-40, 42-48 and 50-70.

The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 23, 25-31 and 33-58 stand rejected as allegedly unpatentable under 35 U.S.C. § 103(a) over Sugiura, Mückter, or Mau'ad. Applicant respectfully traverses this rejection.

Under current law, a prior art reference or references cannot render a claim obvious unless the PTO provides evidence that the reference or references meet a three-part test for *prima facie* obvious. To begin with, the prior art reference or references must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002). Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, "[b]oth the suggestion and the reasonable expectation of success 'must be

founded in the prior art, not in the applicant's disclosure.'" *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996).

In this case, Applicant respectfully submits that the Examiner has not shown that, prior to this invention, the cited references would have provided any suggestion of the claimed invention, or motivation to modify or combine the cited references to arrive at the claimed invention. Further, the references fail to suggest each and every claim element, much less provide a reasonable expectation of success.

Sugiura Fails to Render the Claims Obvious

The Examiner contends that it is not persuasive for Applicant to argue that "Sugiura does not teach what cancer thalidomide might be used for and that at most, [Sugiura] is an invitation to experiment with thalidomide in certain unknown cancer cases." (Page 2 of Office Action). Applicant respectfully disagree.

The Examiner alleges that "Sugiura disclosed that thalidomide had a moderate inhibitory effect on Lewis bladder carcinoma (page 59) and slight inhibiting effect on 6 other tumors. This would render it obvious to use for at least these tumors, especially in patients for whom other treatments had not been successful." (Page 2 of Office Action, emphasis added). Applicant respectfully points out that the Examiner's very statement demonstrates lacks of the legally required suggestion and expectation of success. Indeed, the Examiner has in essence erroneously equated "obvious to try" with "obviousness" under 35 U.S.C. § 103(a). As the Examiner is aware, an allegation that something may have been "obvious to try" cannot form an adequate basis for a obviousness rejection under § 103. *In re O'Farrel* 853 F.2d 894, 57 USLW 2147, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

Sugiura discloses that thalidomide had a only moderate inhibitory effect on Lewis bladder carcinoma when repeatedly injected with the significantly high doses of 1,000mg/kg/day, but had practically no inhibitory effect on the growth of 24 other mouse, rat and hamster tumors. (Synopsis, page 57 and Table 1, page 59). Because the results of Sugiura are so poor and no significant degree of antineoplastic activity was demonstrated in animals, much less in humans, Sugiura fails to suggest to those of ordinary skill in the art that

they should carry out the claimed methods, particularly using the doses recited in claims 27-29. Sugiura does not teach or suggest how to obtain desired results in human cancer patients, or that the claimed invention would be obtained if certain experimentations were performed.

At most, Sugiura provides a mere invitation to experiment on more animals with different cancers in the hope of obtaining better results. Sugiura may arouse the scientist's curiosity with a possibility that a particular type of cancer may show some degree of response and suggest a reason to try thalidomide to determine its efficacy against cancer. However, in Sugiura, further trials of thalidomide in humans are not indicated. *In re Eli Lilly & Co.,* 902 F.2d 943, 945 (Fed. Cir. 1990) ("An 'obvious to try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain direction were pursued"). This "obvious to try" is not a legitimate test of obviousness. *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). *See also Novo Nordisk A/S v. Becton Dickinson and Co.*, 304 F.3d 1216, 1219 (Fed. Cir. 2002).

Further, from the disclosure in Sugiura that thalidomide had practically no inhibitory effect on the growth of 24 mouse, rat and hamster tumors, but only a moderate inhibitory effect on Lewis bladder carcinoma, one of ordinary skill in the art would not have taken any expectation of successfully practicing the claimed invention in inhibiting the formation or growth of tumors in humans, much less at the doses or in the cancer patients claimed in claims 27-29 and 34. Those skilled in the art would interpret Sugiura's teaching as that thalidomide would <u>not</u> be effective in inhibiting tumor formation or growth in humans. This interpretation is evidenced by Mückter which cites Sugiura's test results and describes that "in nearly all of the experiments, no indication of cytostatic action of thalidomide was observed." (Table 1, page 531 of Mückter). This interpretation is the very and actual evidence of what a person of ordinary skill in the art thought of teachings of Sugiura. In determining a *prima facie* case of obviousness, the Patent Office cannot ignore and must consider what one of ordinary skill in the art would interpret the reference. Therefore, one skilled in the art would not have been motivated to use thalidomide in the claimed methods in humans.

In sum, the Examiner has not shown that Sugiura provided those skilled in the art with any suggestion of the claimed invention, motivation to modify the cited reference, much less with the legally required reasonable expectation of success. Thus, the obviousness rejection over Sugiura must be withdrawn.

Mückter Cannot Support the Obviousness Rejection

The Examiner has maintained the rejection of claims 23, 25-31 and 33-58 as allegedly unpatentable under 35 U.S.C. § 103(a) over Mückter. (Page 2 of the Office Action). The Examiner alleges that Sprague Dawley rats were considered relevant models for the study of breast cancer, as seen in the publications by Ace Animals, Inc. and Medline, and that Applicant's argument, that the animal studies and results as set forth in Mückter do not suggest the claimed invention, is not persuasive. (Pages 2-3 of the Office Action). Applicant respectfully traverses this rejection.

All the references cited by the Examiner to show that Sprague Dawley rats were considered relevant models do not change the fact that Mückter does not suggest Applicant's invention. None of the references relate to use of thalidomide, and do not teach or suggest the claimed inventions.[1] At most, the publication and Medline references merely show that Sprague Dawley rats were popularly used in animal experiments for cancer.

Mückter experimented on two types of animals: rats for hormone-dependent tumors induced by 7,12-dimethylbenzanthracence (DMBA), and mice for spontaneously developing mammary carcinomas. In experiments on rats, thalidomide showed some responses in delaying the appearance and growth of tumors over a period of four or five weeks limits. (See pages 533-535 of Mückter). However, the actions of thalidomide in rats definitely abated after about six months of treatment, and the tumors grew again at rates comparable with those of the controls. (Page 536, left and right columns, and page 537, left column of Mückter). Also, the effect is limited by the size of the tumor at the time of first administration of the drug, and by the duration of the treatment. (*Id.*) Thus, Mückter would not have provided one of ordinary skill in the art with the legally required suggestion or reasonable expectation of success that thalidomide is effective against tumors in animals, much less in humans at the doses recited in claims 27-29.

Further, in experimenting on mice with spontaneously developing mammary carcinomas, Mückter reports that thalidomide did not influence either the number or the growth of tumors in mice, and that the survival time of mice was not significantly influenced by thalidomide. (Figures 11 and 12 , pages 537-538 of Mückter). Therefore, the reference as a whole cannot be interpreted as suggesting that thalidomide is effective against cancers.

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[1] The 2004 publication by Ace Animals, Inc. cannot be used as a prior art against the claimed invention because the publication date is after the filing date of the present application, *i.e.*, March 1, 1993.

This disclosure would not have provided one of ordinary skill in the art with a reasonable expectation of success in practicing the claimed methods even in animals, much less in humans. From the disclosure, one of ordinary skill in the art would not have been motivated to combine or modify the reference to arrive at the claimed invention. Simply put, Mückter actually teaches away from the claimed invention. (*Id.*) Applicant respectfully asserts that the Examiner cannot consider only selected teachings in the art, improperly ignoring disclosures that teaches away. The Examiner must consider the art as a whole. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d at 1531 (Fed. Cir. 1988).

For the above reasons, Applicant respectfully submits that Mückter cannot support the obviousness rejection.

Mau'ad Fails to Suggest the Claimed Invention

Claims 23, 25-31 and 33-58 were rejected as allegedly unpatentable under 35 U.S.C. § 103(a) over Mau'ad. The Examiner contends that Mau'ad (pages 16-32, English translation) discloses that thalidomide is effective against many different kinds of cancer. (Page 3 of the Office Action).

Contrary to the Examiner's contention, Mau'ad does not teach or suggest that the single use of thalidomide is effective against any kinds of cancer. Mau'ad tested the effects of the combinations of thalidomide, glucocorticoid, testosterone, dried thyroid, cell permeators and anabolics in cancer patients. (Our Regime on page 11 of the English translation). Mau'ad never used any agent alone (*Id.*), nor obtained any successful result from the single agent of thalidomide. Mau'ad provides no teaching or suggestion that the thalidomide's use resulted in successful treatments of cancer. Without such teachings or suggestions, the Examiner's unsupported statement is nothing but conclusory opinion, and it cannot form a basis for obviousness rejection. *In re Sang-Su Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002) ("A *prima facie* case of obviousness must be satisfied with factual and objective evidence found in the prior art"). Further, the prior art does not provide one of ordinary skill in the art with a reasonable expectation of success of practicing the claimed invention using thalidomide. Thus, Applicant respectfully requests that the rejection over Mau'ad be withdrawn.

Prior Art as a Whole Teaches Away From the Claimed Invention

The Examiner further finds unpersuasive Applicant's argument that there is no motivation to use thalidomide to treat cancer in light of the disclosures of the art as a whole. The Examiner contends that "there are sufficient teachings in the art, as cited above, to render

it obvious to one of ordinary skill in the art to use thalidomide to treat cancer." (Page 3 of the Office Action). This statement, which is made without factual support,[2] is contrary to the disclosures of prior art as a whole. The Examiner has cited no portion of any prior art suggesting or providing a reasonable expectation of success that thalidomide is effective against any cancer in humans. The examiner's unsupported and conclusory statements cannot support a rejection under § 103. *In re Sang-Su Lee*, 277 F.3d at 1343-4.

Applicant submitted several published articles in its Information Disclosure Statements disclosing that thalidomide was not useful for a treatment of cancer, *i.e.*, C1 (Sugiura), C2 (Mückter), C3 (Grabstald, over which the Examiner withdrew the rejection in the outstanding Office Action) and C4-C13. Applicant discussed each reference of record in Response submitted on January 27, 2005.

Applicant further submits a Supplemental Information Disclosure Statement with several published articles which were found after receiving the outstanding office action and have not been considered by the Examiner. Applicant respectfully requests that the Examiner consider and enter these new references in the record of this application.

First, Applicant directs the Examiner's attention to Koch, *Progress in Medicinal Chemistry*, Vol. 22, 1985, pages 165-242, "Thalidomide and Congeners as Anti-inflammatory Agents." In particular, Koch cites and discusses several publications relating to the activity of thalidomide in tumors at pages 181-184.

Koch discloses that articles exist that, contrary to the claimed invention, suggest that thalidomide has cancer-promoting or carcinogenic activity. *Id.*, page 184. For example, Miura *et al.* reported that thalidomide had a potentiating effect on methylcholanthrene oncogenesis in mice. M. Miura, C.M. Southam and H. Wuest, *Experientia*, 26 (1970), page 305-306. Roe and Mitchley tested thalidomide for potential carcinogenicity and found well-differentiated spindle cell sarcomas at the injection site in some of mice. F.J.C. Roe and B. C.V. Mitchley, *Nature*, December 7, 1963, Volume 200, page 1016-17, "Thalidomide and Neoplasia." Miller *et al.* reported that a 15-year-old patient with thalidomide-induced malformations developed a lymphoma of high malignancy. A. Miller, C.G. Schmidt, A. Horwitz and W. Kosenow, *Monatsschr. Kinderheilk.*, 128 (1980) 27-29. Thus, one skilled in the art reading these articles would not use thalidomide for treating or preventing tumors, as claimed herein.

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[2] To the extent these assertions are based on the Examiner's personal knowledge, Applicants respectfully request that such knowledge be supported by an affidavit. 37 C.F.R. § 1.104(d)(2).

Koch also cites several publications reporting on research on the anti-tumor activity of thalidomide and concludes that anti-tumor activity of thalidomide remains doubtful. *Id.*, page 184. This interpretation would be the actual evidence of what a person of ordinary skill in the art thought of prior art. Thus, one skilled in the art reading Koch would interpret that thalidomide would not be effective in inhibiting tumor formation or growth in humans as recited in the claimed invention.

For example, Koch discloses that Allegri treated twelve patients with various malignant tumors with thalidomide at doses from 50 mg to 1.05 g per day for periods of between 6 and 37 days, but there was no visible anti-tumor effect. Koch at 181; A. Allegri, *Gazz. Med. Ital.*, 123 (1964), 124-127.

Further, Woodyatt, *Lancet*, 1962, page 750, "Thalidomide" discloses that a woman having a malignant mixed mesodermal tumor of endometrium was treated with thalidomide but the tumor growth has not regressed, and that in fact there may have been a very slight increase in size. *Id.*

Traldi *et al.* reported that thalidomide was given to patients with malignant neoplastic diseases (gastric cancer, lymphoblastoma) and it had no influence on the neoplasm itself in all of these patients. A. Traldi, G.L. Vaccari and G. Davoli, *Cancro*, 18 (1965), 336-341.

Thus, all of these studies failed to provide any promise for thalidomide as effective in inhibiting the formation or growth of tumors in humans. The studies neither provide with any suggestion, nor a reasonable expectation of success in inhibiting tumors in humans.

The reported inefficacy of thalidomide as an anti-tumor agent prior to the claimed invention had been reportedly confirmed in various animal experiments and in cell cultures. Juret *et al.* experimented an Ehrlich ascites tumor in the mouse and a solid epithelioma in the rat but could not find any suppressive activity of thalidomide. Koch at 182; P. Juret *et al.*, *Seances Soc. Biol. Filial.*, 157 (1963), 246-249. Pagnini *et al.* studied the effect of thalidomide upon two experimental tumors, Ehrlich ascites carcinoma in the mouse and myeloma in the rat, but no significant change in the mortality rates of the treated animals and the controls was found. Koch at 180; G. Pagnini and R. Di Carlo, *Boll. Soc. Ital. Biol. Sperim.*, 39 (1963), 1360-63. Gaetani tested thalidomide to tumor-inoculated mice and found no influence of the drug upon development of various tumors such as Ehrlich ascites, myeloma, sarcoma and transplantable teratoma. Koch at page 183; M. Gaetani, *Giorn. Ital. Chimioter.*, 11 (1964), 83-86.

In view of the foregoing, the prior art as a whole would not have provided one of ordinary skill in the art with any suggestion or a reasonable expectation of success in

practicing the claimed methods in animals, much less in humans. Further, one of ordinary skill in the art would not have been motivated to combine or modify any references to arrive at the claimed invention.

In order to help the Examiner understand the prior art as a whole, Applicant summarizes the test results of the relevant publications and submits them as Exhibit A.[3]

As summarized in the Exhibit, the prior art as a whole indicates that thalidomide was not successful in inhibiting tumors in animals and humans. Thus, the prior art does not render it obvious to one of ordinary skill in the art to use thalidomide to treat cancer as in the claimed invention. The prior art as a whole fails to provide the requisite legal suggestion or reasonable expectation of success. For these reasons, the obviousness rejection should be withdrawn.

The Rejection Under Obviousness-Type Double Patenting Should Be Withdrawn

Claims 23, 25-31 and 33-58 stand rejected under the judicially created obviousness-type double patenting over claim 1 of U.S. Patent No. 5,629,327 ("the '327 patent"). (Page 4 of the Office Action). The Examiner alleges that the conflicting claims are not patentably distinct from each other, because '327 patent discloses a method of using thalidomide to treat undesired angiogenesis for the reasons given in the Office Action of July 27, 2004.

Without acquiescing in the Examiner's rejection, Applicant submits herewith a Terminal Disclaimer under 37 C.F.R. § 1.321(b) by the assignee of the present application (1) disclaiming any part of any patent granted on this application which could extend beyond the expiration date of the '327 patent; and (2) ensuring that any such patent granted on the application shall be enforceable only for and during such period that such patent is commonly owned with the '327 patent.

Applicant submits that the submission of the Terminal Disclaimer obviates the rejection based on obviousness-type double patenting, and respectfully requests its withdrawal.

Applicant Properly Submitted Bach, The Lancet

The Examiner further finds that Bach, The Lancet, could not be considered since it was not received. (Page 5 of the Office Action). On January 27, 2005, Applicant submitted a

[3] Each of these references is available for the Examiner's review in the record. Applicants submit copies of the references and will provide the translations when the Examiner requests such.

copy of the reference as C7, Bach, *The Lancet*, June 8, 1963, No. 71, page 1271, "Thalidomide in Cancer Chemotherapy." Applicant again submits another copy of the same reference and respectfully requests that the Examiner review the reference and make a record of the reference in the file history of the application.

Conclusion

Applicant respectfully requests that the above remarks be entered in the file of this application. Should the Examiner not agree that all claims are allowable, then a further personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application. Please charge any required fees to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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EXHIBIT A: SUMMARY OF REFERENCES

IDS #	Reference	Study	Result
C1	Sugiura et al., *GANN*, 1964, No. 55, pp. 57-60, "Effect of Thalidomide on Transplantable Mouse, Rat and Hamster Tumors"	*In Vivo* (Transplantable mouse, rat and hamster tumors)	18 ***No*** inhibition, 6 slight (sarcoma, Ehrlich carcinoma, Lewis lung carcinoma, Harding-Passey melanoma, Walker rat carcinosarcoma, Jensen rat sarcoma), and 1 moderate inhibition (Lewis bladder carcinoma)
C2	Mückter, *Antimicrobial Agents and Chemotherapy*, 1965, pp. 531-538, "Thalidomide and Tumors"	*In Vivo* (DMBA-induced tumors in rats, and spontaneously developing mammary carcinomas in mice)	***In***effective in mice, responded in rats for 4-5 weeks treatment but no response after 6 week
C3	Grabstald *et al.*, *Clinical Pharmacology and Therapeutics*, 1965, No. 6, pp. 298-302, "Clinical Experiences with Thalidomide in Patients with Cancer"	71 human patients with cancers of kidney, bladder, testes, prostate, gynecology, breast, digestive tract, parotid, lung, lymphoma, multiple myeloma, thyroid, gingiva and sarcomas	***In***effective except one renal cancer patient who had nephrectomy
C4	Joseph A. DiPaolo, *Cancer Chemotherapy Reports*, May 1963, No. 29, pp. 99-102, "Effect of Thalidomide on a Variety of Transplantable Tumors"	*In Vivo* (transplatable standard mouse and rat tumors; Ridgway osteogenic sarcoma and teratocarcinoma in mice, rhabdomyosarcoma in rats, and choriocarcinoma in hamsters)	***In***effective
C5	Joseph A. DiPaolo, *Proceedings of the Society for Experimental Biology & Medicine*, 1963, v114, pp. 384-387, "*In vitro* Test Systems for Cancer Chemotherapy, II. Correlation of *in vitro* Inhibition of Dehydrogenase and Growth with *in vivo* Inhibition of Ehrlich Asoites Tumor"	*In Vitro* and *In Vivo* (Ehrlich ascites tumor grown in mice)	***In***effective
C6	Joseph A. DiPaolo, *Science*, June 26, 1964, p. 1583, "Thalidomide: Effects on Ehrlich Ascites Tumor Cells *in vitro*"	*In Vitro* (Ehrlich ascites tumor)	***In***effective
C7	A. Bach, *The Lancet*, June 8, 1963, No. 71, p. 1271, "Thalidomide in Cancer Chemotherapy"	*In Vivo* (mice with transplantable adenocarcinoma and stem-cell leukemia)	***In***effective
C8	A. Bach, *Acta Pathologica Et Microbiologica Scandinavica*, 1963 (59), pp. 491-499, "Studies on the Possible Anti-Neoplastic Effect of Thalidomide"	*In Vivo* (transplantable mouse tumors)	***In***effective
C9	F. J. C. Roe and B. C. V. Mitchley, *Nature*, December 7, 1963, Volume 200, pp. 1016-17, "Thalidomide and Neoplasia"	*In Vivo* (sarcoma in mice)	***Carcinogenesis*** of sarcoma
C10	Chaundhry, *Cancer Research*, 1966, 26 part 1, 1884-86, "Effect of Prednisolone and Thalidomide on Induced Submandibular Gland Tumors in Hamster"	*In Vivo* (fibrosarcoma in hamsters)	***In***effective
C11	Gershbein, *Cancer Letters*, 1991, 60:129-133, "The thalidomide analog, EM 12, Enhances 1,2-Dimethylhydrazine-Induction of Rat Colon Adenocarcinomas"	*In Vivo* (colon adenocarcinomas in rats)	***In***effective
C12	Olson *et al.*, *Clinical Pharmacology and Therapeutics*, 1965, 6(3):292-297, "Thalidomide (N-phthaloylglutamimide) in the treatment of advanced cancer"	21 human patients with 14 types of cancers (kidney, parotid, ovary, breast, melanoma, thyroid, lung, multiple myeloma, chondrosarcoma,	***No*** objective evidence of tumor regression

IDS #	Reference	Study	Result
		fibrosarcoma, reticulum cell sarcoma, mesenchymoma, liposarcoma, and rhabomyosarcoma)	
C13	MAU'AD MJ., Anais *Paulistas de Medicinae Cirurgia*, 1963, 86:13-40, "Clinical Improvements Obtained in Advanced Caner Patients with Treatment with Thalidomide Associated with Hormones"	22 malign and 3 benign tumor patients	Effective by combination, but *no test performed with thalidomide alone*
C14	Koch, *Progress in Medicinal Chemistry*, Vol. 22, 1985, pages 165-242, "Thalidomide and Congeners as Anti-inflammatory Agents"	Discussed various articles on tumor studies	Anti-tumor activity *doubtful*
C15	M. Miura, C.M. Southam and H. Wuest, Experientia, 26 (1970), 305-306	Mice	***Carcinogenesis*** of skin papillomas
C16	A. Miller, C.G. Schmidt, A. Horwitz and W. Kosenow, Monatsschr. Kinderheilk., 128 (1980) 27-29	Human patient	***Carcinogenesis*** of lymphoma
C17	A. Allegri, *Gazz. Med. Ital.*, 123 (1964), 124-127	Human patients (various malignant tumors)	***In***effective
C18	P. B. Woodyatt, *Lancet*, 1962, page 750, "Thalidomide"	Human patient (mesodermal tumor of endometrium)	***In***effective
C19	A. Traldi, G.L. Vaccari and G. Davoli, *Cancro*, 18 (1965), 336-341	Human patient (gastric cancer and lymphoblastoma)	***In***effective
C20	P. Juret *et al.*, *Seances Soc. Biol. Filial.*, 157 (1963), 246-249	Ehrlich ascites tumor in mouse and a solid epithelioma in rat	***In***effective
C21	G. Pagnini and R. Di Carlo, *Boll. Soc. Ital. Biol. Sperim.*, 39 (1963), 1360-63	Ehrlich ascites carcinoma in mouse and myeloma in rat	***In***effective
C22	M. Gaetani, *Giorn. Ital. Chimioter.*, 11 (1964), 83-86	Mice (Ehrlich ascites, myeloma, sarcoma and transplantable teratoma)	***In***effective